Product Data Sheet

Chemical Properties

Product Name: Tosedostat (CHR2797)
Cas No.: 238750-77-1
M.Wt: 406.47
Formula: C21H30N2O6
Chemical Name: cyclopentyl (2S)-2-[(2R)-2-[(1S)-1-hydroxy-2-(hydroxyamino)-2-oxoethyl]-4-methylpentanoyl]amino]-2-phenylacetate
Canonical SMILES: CC(C)(C(C(=O)NO)O)C(=O)NC(C1=CC=CC=C1)C(=O)OC2CCCC2
Solubility: ≥40.6 mg/mL in DMSO, ≥15.07 mg/mL in EtOH with ultrasonic, <2.53 mg/mL in H2O
Storage: Store at -20°C
General tips: For obtaining a higher solubility, please warm the tube at 37°C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.
Shopping Condition: Evaluation sample solution: ship with blue ice
All other available size: ship with RT, or blue ice upon request

Biological Activity

Targets: Metabolism
Pathways: Aminopeptidase
Description:

Tosedostat is a novel and potent oral aminopeptidase inhibitor with clinical activity in a previous phase 1–2 study in elderly patients with relapsed or refractory acute myeloid leukaemia (AML).[2]

Aminopeptidases play a key role in the protein cell cycle. Inhibition of aminopeptidase results in the amino acid deprivation response, which occurs selectively in transformed cells and leads to upregulation of proapoptotic factors including CHOP and NOXA, activation of stress-related
pathways such as NFκB, and inhibition of mTOR, which switches off protein synthesis. [2]
Tosedostat (CHR-2797) is converted intracellularly into a pharmacologically active metabolite
CHR-79888. [1]
Tosedostat has antiproliferative, antiangiogenic and proapoptotic effects. Tosedostat is currently
in a clinical trial phase for anticancer therapy, and displayed a broad antifungal activity against
different Candida spp, including Candida glabrata. Tosedostat depletes sensitive tumour cells of
amino acids by blocking protein recycling and thereby generates an antiproliferative effect.
Tosedostat has activity in older patients with relapsed or refractory AML. [2]

Reference:
1.Van Herpen CM, Eskens FA, de Jonge M et al. A Phase Ib dose-escalation study to evaluate
safety and tolerability of the addition of the aminopeptidase inhibitor tosedostat (CHR-2797) to
2.Cortes J, Feldman E, Yee K et al. Two dosing regimens of tosedostat in elderly patients with
relapsed or refractory acute myeloid leukaemia (OPAL): a randomised open-label phase 2 study.

Protocol

Cell experiment:

Cell lines Human multiple myeloma (MM) cells
Preparation method The solubility of this compound in DMSO is > 10 mM. General tips
for obtaining a higher concentration: Please warm the tube at 37 °C
for 10 minutes and/or shake it in the ultrasonic bath for a while.
Stock solution can be stored below -20 °C for several months.

Reactive conditions

Applications CHR2797 showed antiproliferative and apoptotic effects against MM
in vitro by inducing the AA deprivation response (AADR). Using MTS
and CTG assays, CHR2797, at clinically achievable concentrations,
decreased survival and proliferation in MM1S and IL-6-dependent
ANBL6 cells, in the presence or absence of bone marrow stromal
cells following 72 hours incubation. CHR2797 induced apoptosis in
MM cells via activation of Caspase 3/7 and 9 but not Caspase 8.
CHR2797 (10 μM) induced apoptosis in patient MM cells. Combined
 treatment with CHR2797 and LBH589 in MM cells (MM1S, ANBL6,
and INA6) further reduced cell viability following 72 hour incubation
when compared with CHR2797 treatment alone. CHR2797 (1 μM) in
combination with LBH589 (1 nM) showed an increased growth
arrest in G0/G1 cells in MM1R cells treated with both drugs versus
CHR2797 alone after 24 hours. CHR2797 inhibited anti-apoptotic
protein Mcl-1 in MM1R and U266 MM cells.
Reference:

Product Citations


Caution

FOR RESEARCH PURPOSES ONLY.

NOT FOR HUMAN, VETERINARY DIAGNOSTIC OR THERAPEUTIC USE.

Specific storage and handling information for each product is indicated on the product datasheet. Most ApexBio products are stable under the recommended conditions. Products are sometimes shipped at a temperature that differs from the recommended storage temperature. Short term storage of many products are stable in the short-term at temperatures that differ from that required for long-term storage. We ensure that the product is shipped under conditions that will maintain the quality of the reagents. Upon receipt of the product, follow the storage recommendations on the product data sheet.